6.1 Cystic Fibrosis (CF)- Follow-up of Positives

POLICY: All CF recall testing (via sweat chloride test) is to be conducted by a CCS-Certified and Cystic Fibrosis Foundation (CFF)-Approved Cystic Fibrosis Center using a CFF- approved lab.

GUIDELINES FOR INITIAL POSITIVES: **An initial positive can be either** a case with an immunoreactive trypsinogen (IRT) value equal to or over 62 ng/ml and 2 DNA mutations or potentially disease-causing variants in the cystic fibrosis gene, **or** a case with a high IRT, one CF mutation, and a 12TG-5T or 13TG-5T variant identified in the CF gene. *

- Infants with a high IRT will have their blood spots sent to Stanford University Medical Center Molecular Pathology Laboratory for CF DNA mutation panel testing. If two mutations are identified the case will be reported as an initial positive on the Headline Case list.
- If only one mutation is identified on the DNA panel, the Stanford Molecular Pathology Lab will perform CF DNA sequencing. The initial results mailer, which has "Additional Results Pending" printed in a purple box at the top, is sent out to the birth hospital and doctor of record with the high IRT result and the name of the mutation for CF identified by the DNA panel, noting that the specimen is undergoing further DNA testing for CF. DNA sequencing takes about 2 weeks. Unless the infant is screen positive for another disorder at this point, the case does not appear on the ASC Headline Cases.
- If sequencing identifies a second mutation or potentially disease-causing variant, the case is reported out as "positive for CF or a CFTR-related disorder". A DNA sequencing result mailer with information on the known clinical implications of the mutations and variants will be sent to the birth hospital and physician. **On the SIS Case Summary** page Test Results grid, the CFTR Mutation Panel interpretation is "Incomplete" and the CFTR DNA Sequencing interpretation is **"**Referred"; this means a second mutation was identified and this is a CF screen positive that needs to be referred to a CF Center. **Clicking on "CFTR DNA Sequencing" brings up the CF Test Results page** with a description of the mutations identified and the interpretation.

NOTE: Physicians receiving an initial mailer with a high IRT and one CF panel mutation may inquire about referring babies for sweat testing immediately, rather than waiting for the DNA sequencing results. The NBS Program recommends waiting for the sequencing results before requesting sweat testing unless the baby has clinical symptoms of CF, the parents are known carriers of CF, or there is a family history of CF. About 1/3 of the specimens sequenced have a second CF mutation or potentially disease-causing variant, and are interpreted as CF positive; about 2/3 will not have a second mutation/significant variant identified, with results interpreted as consistent with the infant being a CF carrier.

*Results with one CF mutation and an 11TG-5T variant are reported out as CF carriers, and will not be ASC Headline Cases, effective 6-1-11.

Attachments:

3.15.1 A Minimum Guidelines for Follow-up of Newborns with Positive Cystic Fibrosis Newborn Screening Results
3.15.1 B CF Fact Sheet – 2 Mutations
3.15.1 C ASC Guide for Questions from Providers on NBS CF Results of: Elevated IRT and Negative CFTR DNA Panel
3.15.1 D CF Mailer Wording

6.1 Cystic Fibrosis (CF)- Follow-up of Positives

PROTOCOL:

Resp. Person	Action
ASC NBS Coord. or Program Specialist	• **Daily** reviews the Daily Report (Headline Case Report) for CF positive cases. • **Within 48 hours of obtaining a positive result for CF,** calls newborn's physician (and the hospital, if infant is still hospitalized) with results. Discusses immediate referral to a CCS-approved CF Special Care Center for evaluation and sweat testing. • Assists physician with referral to appropriate CF Center (See protocol for Referral to CCS Centers). Requests information from the physician regarding which CF Center is a preferred provider for the family's insurance. If the preferred Center is too distant, a referral can be made to the closest Center. • Unless primary care physician objects, contacts the CF Center to notify staff of referral. • Documents all attempts at notification, interactions with physicians and parents using tracking events or case notes in SIS. • Faxes/Sends follow-up letter to physician confirming the CF results for the baby and referral information, along with the CF fact sheet for providers. • If the baby has been discharged from the hospital, and parents have been contacted by the physician about the NBS CF results, sends a letter to the parents notifying them of the need for referral to a CCS-approved CF Special Care Center and includes the brochure *"Cystic Fibrosis in Babies".* • Makes referral to CCS per protocol. • **If the physician or ASC Coordinator is unable to contact the parents within one week after the first call to the physician**, sends letter notifying parents to call the physician about baby's test results. Parent letter shall be sent by regular 1st class mail and a second copy sent by Certified Receipt mail requested to maximize receipt by parent. • **If contact still not made in one week after sending parent letter**, makes arrangements for a home visit by the local Health Department Public Health Nurse. • Contacts CF center regularly (at least monthly unless informed via 'SIS or phone that baby will not be seen for over a month) to track status of case, and documents findings in SIS. • Follows case until resolved as "Suspect CF"/CRMS*, "Confirmed CF" or "CF No disorder/Carrier" by the CF Center and the sweat test results have been entered in SIS Confirmatory Test Results. *Cystic Fibrosis-Related Metabolic Syndrome

6.1 Cystic Fibrosis (CF)- Follow-up of Positives

- **If after 9 months from accession date, the CF specialist has not arrived at a resolution:**
  -Contacts the specialist to inquire if a diagnosis had been made and informs him/her that ASC staff will no longer be tracking case but that state staff will be contacting him/her periodically to obtain required case outcome information.

  -Sends letter (320.C) to specialist stating same.

  -Transfers case to designated PDEB CF Monitor (CCC 102) via "Re-assign CCC"screen in SIS.

- Documents all attempts at notification, interactions with physicians and parents using tracking events and/or case notes in SIS.

- Reports unusual occurrences such as missed cases (e.g., with meconium ileus and positive sweat test), anomalous/inconsistent results, cases diagnosed by prenatal screening or missed screening after 7/1/07 due to parent refusal, military birth hospital or out-of-state birth to the NBS Nurse Consultant coordinating Anomalous Results investigations and the PDEB CF Monitor.

- Reports lost to follow-up cases, delays in contacting family, delays in analysis or reporting of sweat test results, etc., of potential significance to the NBS ASC Contract Liaison /Nurse Consultant .

- Refers case to Child Protective Services as appropriate and with approval of NBS Nurse Consultant/Contract Liaison.

- Requests documentation of diagnosis in SIS by the CF Center, if not completed on the Cystic Fibrosis Service Record (CFSR) and in Confirmatory Test Results in SIS.

- Resolves case on Case Resolution Screen in SIS.
  If the infant expires, is lost to follow-up, or parent refuses/is non-compliant with testing or follow-up before a diagnosis can be made, resolves the case as follows:
  (1) If the infant had 2 mutations identified by the panel, the case should be resolved as: Disorder. Choose reliability code of "Probable".
  (2) If the infant had 1 mutation identified by the mutation panel and 1 (or more) mutation(s)/variants identified by sequencing, the case should be resolved as: Disorder and Suspect Cystic Fibrosis/CRMS. Choose the reliability code of "Tentative".

- Calls the GDSP CF Monitor with reports new CF cases not screened in the California NBS program (e.g., born prior to screening or born out of state).

6.1 Cystic Fibrosis (CF)- Follow-up of Positives

CF Center	• Daily checks Cases Referred in SIS for new referrals and accepts referrals from ASCs or GDSP. Schedules baby and family to be seen at next available clinic appointment, or earlier if medically indicated. Documents appointment date in SIS Case Notes. • Contacts PCP to discuss health status of newborn. • At initial visit assists parent/guardian with completion of CCS application per CCS policy and faxes completed application to local CCS office. • Orders confirmatory/diagnostic laboratory testing as appropriate to confirm or rule out a diagnosis. Sweat testing is to be done only in Cystic Fibrosis Foundation-Approved labs. • Provides primary care physician with information on laboratory results and any necessary follow-up within 24 hours of receiving results. • Enters the sweat chloride results in SIS (in "Confirmatory Test Results"). • Faxes copies of lab reports with the results of CF DNA mutation analysis of the newborn's parents or additional mutations found in the newborn to the GDSP CF Monitor for entry into SIS. • Bills family's insurance and/or CCS for services at CF Center per CCS guidelines. • Bills CCS for diagnostic services per CCS guidelines. • Develops treatment plan. • Sends follow-up letter to the physician, confirming physician notification and recommendations. • Enters Cystic Fibrosis Service Record (CFSR), and case notes, if appropriate, into SIS within one business day and no later than 5 calendar days after each significant contact until the diagnosis is confirmed and a treatment plan is initiated. • Documents missed and rescheduled initial evaluation appointments in Case Notes in SIS; notifies the ASC as early as possible, and no later than 5 days after the occurrence. • Following sweat test and diagnostic evaluation, resolves case according to the *Minimum Guidelines for Follow-up of Newborns with Positive Cystic Fibrosis Newborn Screening Results* (see 3.15.1 A). • Upon request, provides consultation to ASC and GDSP staff, newborns' primary care physicians, neonatologists, and/or CCS authorizing agency regarding diagnosis and treatment of cystic fibrosis.